Review Article

Myocardial Revascularization without Extracorporeal Circulation; Why Hasn't It Convinced Yet?

Abstract

Extracorporeal circulation has led to a great development in cardiovascular surgery during the last five decades. Its time-proven efficacy and safety have made on-pump coronary artery bypass grafting (CABG) the gold standard method of surgical revascularization. However, coronary revascularization on cardiopulmonary bypass and the accompanying aortic manipulation are related to plenty of deleterious complications. Therefore, off-pump CABG surgery was established to avoid complications. Nevertheless, despite the initial enthusiasm on this technique, only 20% of myocardial revascularization procedures worldwide are performed off-pump. Not only are off-pump cardiac procedures more technically difficult but also they do not provide better results in terms of graft patency, completeness of revascularization, repeat revascularization requirement, cost, and quality of life. Completeness of revascularization and anastomotic quality should not be compromised to avoid cardiopulmonary bypass.

Keywords: *Coronary artery bypass grafting, off-pump, on-pump, myocardial revascularization*

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Introduction

Thorough comparisons between on-pump (ONCAB) and off-pump (OPCAB) coronary artery bypass surgery have not managed to answer which is the ideal surgical strategy yet.[1] Certainly, extracorporeal circulation has led to a great development in cardiovascular surgery during the last five decades. Its time-proven efficacy and safety have made ONCAB the gold standard method of surgical revascularization.[2] However, coronary revascularization on cardiopulmonary bypass (CPB) and the accompanying aortic manipulation are related to plenty of complications, such as myocardial ischemic injury, coagulation disorders, neurocognitive deficits, strokes, complement activation, and systemic inflammatory response which may lead to renal failure, pulmonary, or hematologic complications.[1,2] These deleterious effects of CPB and aortic manipulation were the reasons why coronary artery bypass grafting (CABG) without the use of extracorporeal circulation, the so-called OPCAB was established.[1] OPCAB, having the potential to decrease perioperative morbidity, mortality, and cost, expanded worldwide; and nowadays, some centers have adopted it as the method of choice for the treatment of coronary artery disease.[2] Indeed, 95% of cardiac revascularization procedures in India are performed off-pump, whereas 25% of them concerned OPCAB in North America in 2004.[3] Nevertheless, despite the initial enthusiasm on OPCAB, a plateau has been reached in recent years, and currently, OPCAB accounts for only 20% of myocardial revascularization procedures worldwide,[4] whereas the heart-lung machine is still used in 80% of them.[1,5] OPCAB is considered a more technically challenging and demanding approach[1,2] but are the difficulty of the technique and the longer learning curve both for the surgeon and the anesthesiologist to put the blame on? Of course not. There are also additional factors that discourage the surgeon from practicing this operation, including graft patency, completeness of revascularization, and repeat revascularization requirement.[1] Herein, we will try to shed light on the disadvantages of OPCAB and to indicate if OPCAB can play a role in the myocardial revascularization field.

Off-pump Coronary Artery Bypass Indications

The indications for OPCAB have expanded through the years as we become more

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experienced and more familiar with the technical difficulties of this method. The International Society for Minimally Invasive Cardiothoracic Surgery recommendations states that perioperative morbidity, neurocognitive dysfunction, and hospitalization are decreased through OPCAB, so high-risk patients having severe ascending aortic calcification, liver disease, renal insufficiency, or other systemic processes should be candidates for OPCAB to reduce morbidity and mortality.[6] According to the American Heart Association Guidelines in 2011,[7] both ONCAB and OPCAB are reasonable, depending on patient's characteristics. Hence, a patient having a heavily calcified ascending aorta can gain profit from OPCAB. On the other hand, the European Guidelines (2010) do not state anything for OPCAB indications.[8] The elderly and the patients with the left main stem coronary artery disease, impaired left ventricular function, a porcelain aorta, right coronary artery disease, non-STEMI, or pulmonary edema are more often candidates for OPCAB.[4] In high-risk patients, such as in very old patients, postoperative neurological complications and intubation duration are increased when on-pump CABG is performed.[9] However, according to Harold Lazar's review published in "Circulation" in 2013, myocardial revascularization through OPCAB can offer a clear profit only in patients with a porcelain or atherosclerotic aorta having an increased risk for aortic trauma or cerebral embolization and in patients with liver failure or cirrhosis, in whom there is a need to avoid prolonged heparinization periods.[2] Finally, high-risk patients might gain profit from OPCAB use.[1]

Quality-quantity of Distal Anastomoses

It is obvious that performing distal anastomoses on a beating heart and in a bloody surgical field is quite more difficult. Surgical conditions provided by OPCAB, such as the hazard of partial occlusion of coronary arteries, the endooccluders placement and the use of CO_2 blowers, are undoubtedly inferior to the nearly ideal conditions ensured during on-pump CABG. Furthermore, during OPCAB, patients are more prone to significant local damage of the vascular endothelium contributing to local thrombosis.[10] In addition, despite advances in OPCAB equipment, inferior and posterolateral coronary vessels are more difficult to be grafted through OPCAB.[2] Such anastomoses require significant heart moving leading to hemodynamic instability, so they may be frequently performed more distally on the coronary branches during OPCAB than during on-pump CABG. As a result, a double risk is noticed: an inevitably smaller diameter anastomosis, thus being more prone to thrombosis, and retrograde flow for a bigger part of the ischemic myocardium. Moreover, a cardiac surgeon more easily excludes a thinner or a having obvious damages coronary vessel from being the target vessel during OPCAB. Therefore, OPCAB is related to a lower mean of distal anastomoses, when compared to on-pump CABG.[11] When 1 diseased vascular segment is not revascularized, no mortality risk increase occurs. Nevertheless, 2 unrevascularized vascular segments lead to significantly increased mortality risk ($P = 0.01$).[2] Shroyer *et al.* reported that OPCAB was related to fewer than originally planned grafts performed in comparison with ONCAB (17.8% vs. 11.1%, $P < 0.001$).[12] Significantly, fewer graft anastomoses per patient in OPCAB versus ONCAB are performed.[6,13]

In-hospital Mortality

None of the two methods seems to be superior with regard to 30-day mortality according to the international literature. No difference in 30-day mortality was reported by Shroyer *et al*. in the largest (2203 patients), multicenter, randomized trial to date comparing OPCAB with ONCAB.[12] Racz *et al*.,[14] retrospectively comparing 59,000 patients who received ONCAB with 9000 patients who received OPCAB, found no difference in 30-day mortality, as well as in risk-adjusted in-hospital mortality. Hannan *et al*.,[15] retrospectively comparing 13889 OPCAB cases versus 35941 ONCAB cases, observed no difference in 30-day mortality. Moreover, OPCAB was accompanied by lower risk-adjusted mortality rates ($P = 0.002$). Nevertheless, the 30-day mortality rate was 9.73% in the 226 patients who were converted from OPCAB to on-pump CABG. Li *et al*.[16] as well as Puskas *et al*.[17] reported a decrease in risk-adjusted operative mortality in their large retrospective studies. No significant difference in terms of in-hospital mortality was either found in many other retrospective studies by Chu *et al*.,[18] by Palmer *et al*.,[19] by Williams *et al*.,[20] and by Sabik *et al*.[21] Similar results have also been extracted by numerous meta-analyses. In a meta-analysis of 57 trials including 5200 patients by Møller *et al*.,[10] no statistically significant difference in mortality between OPCAB and on-pump CABG was noticed. However, the authors reported that approximately 242,000 patients should be included to extract reliable outcomes concerning the real difference between the two approaches in terms of mortality. Similarly, Cheng's *et al*.[22] meta-analysis of 37 nonrandomized trials, including 3369 patients, revealed no statistically significant superiority in 30-day mortality. Neither Feng *et al*.,[23] analyzing 10 randomized trials in approximately 2000 patients, noticed any significant difference between on-pump CABG and OPCAB neither in early (30-day) peri-operative mortality nor in late (12-month) mortality. Furthermore, in a propensity score analysis by Kuss *et al*.[24] comparing the two methods in approximately 123,000 patients, OPCAB was superior to on-pump CABG, having a lower perioperative mortality rate. According to Murzi *et al*.,[25] CPB was an independent predictor of in-hospital mortality (odds ratio 5.74; $P = 0.001$) and OPCAB was associated to lower in-hospital mortality (0.5% vs. 2.9%; $P = 0.001$). Jarral *et al*.[26] observed a significant reduction in 30-day mortality

in patients with left ventricular dysfunction. Finally, Fattouch *et al*.,[27] comparing OPCAB to ONCAB in their prospective study, reported that patients who underwent emergency surgery within 6 h of the onset of symptoms due to ST-segment elevation myocardial infarction (NSTEMI) with cardiogenic shock took advantage of OPCAB in terms of in-hospital mortality.

Early Postoperative Complications

Blood loss

Many randomized studies have shown that blood loss after OPCAB is significantly less than after on-pump CABG. That is the reason why OPCAB requires a significantly smaller number of red packed-cell and clotting-product transfusions.[28-30] Hu *et al*.[31] examining 6665 patients as well as a meta-analysis by Cheng *et al*.[22] have shown a statistically significant less need for transfusion when OPCAB is used. Similar conclusions were extracted by a propensity score analysis by Kuss *et al*.[24] According to Racz *et al*.,[14] reoperation surgery because of bleeding was significantly more frequent after ONCAB (2.2% vs. 1.6%; $P < 0.001$). OPCAB was also more rarely related to reoperation due to bleeding within 30 days of surgery in Reston *et al*.[32] study, including 46,621 patients.

Myocardial injury

Microemboli and the inevitable ischemic time after clamping the aorta are the main harmful effects of extracorporeal circulation on the coronary circulation. Both randomized and nonrandomized, comparative studies have noticed a smaller increase in cardiac enzymes (creatine kinase-MB [CK-MB] and troponin) in the group of OPCAB compared to the group of on-pump CABG.[28-30,33,34] Lower levels of CK-MB and troponin after OPCAB, showing better myocardial preservation, have also been observed.[28-30,33] Fortunately, there is no need for more inotropic support and no difference concerning arrhythmias frequency in the CABG group as it might be expected.[4,35] Neither the meta-analysis by Møller *et al*.[10] including 44 trials and approximately 4300 patients, nor this one by Cheng *et al*.[22] managed to reveal any statistically significant difference concerning the extent of myocardial injury and other early postoperative complications between the two methods. Another study of MRI evaluation of viable myocardium after revascularization, comparing these two approaches, has failed to prove any significant difference between them although hemodynamic markers, such as cardiac biomarkers and end-systolic volume, were better preserved early postoperatively after OPCAB.[36] A propensity score analysis by Kuss *et al*.[24] also showed no statistically significant difference in the frequency of peri- and post-operative myocardial infarction although OPCAB group was superior to on-pump CABG group in terms of need for postoperative inotropic or mechanical support. Finally, neither a clinical trial by Alamanni *et al*.[37] nor the meta-analysis by Wijeysundera *et al*.[38] reported any significant difference between these two methods in the myocardial infarction rate and in residual ischemia rate. No significant difference in the incidence of perioperative myocardial infarction was either reported by Racz *et al*.,[14] Sabik *et al*.,[21] Reston *et al*.,[32] and Afilalo *et al*.[39]

Atrial fibrillation

According to the meta-analysis by Møller *et al*.[10] based on 30 trials including 3600 patients, OPCAB was related to a lower incidence of postoperative atrial fibrillation. A lower postoperative atrial fibrillation rate in favor of OPCAB was also reported by the meta-analysis by Cheng *et al*.[22] examining 3300 patients of 37 randomized studies. Lower incidence of atrial fibrillation in OPCAB group was also reported among 6665 patients studied by Hu *et al*.[31] as well as in 46,621 patients studied by Reston *et al*.[32] However, the propensity score analyses by Kuss *et al*.[24] did not confirm a statistically significant difference in atrial fibrillation occurrence between the two methods.

Neurological and neurocognitive damage

A significantly lower number of microemboli, mainly due to avoiding enboli-producing extracorporeal circulation and maneuvers on the thoracic aorta, has been reported since the beginning of OPCAB application compared to on-pump CABG.[40-42] Indeed, the meta-analysis by Møller *et al*.[10] showed a difference in favor of OPCAB although not statistically significant. No statistically significant difference in the incidence of strokes was either reported by Sabik *et al*.[21] In contrast, a propensity score analyses by Kuss *et al*.[24] reported statistically significant difference in neurological damage in favor of OPCAB. Significantly, higher incidence of stroke in ONCAB group was also reported by Racz *et al*. (2.0% vs. 1.6%; $P = 0.003$).[14] Lower incidence of 30-day cerebrovascular accidents was also reported by Reston *et al*.[32] As far as neurocognitive disorders are concerned, statistically significant higher occurrence has been demonstrated in the on-pump CABG group.[34,43,44] This is especially true in the elderly, where their frequency after on-pump CABG is at least 4-fold that after OPCAB.[9] However, Lamy *et al*.[45] observed in the Coronary Artery Bypass Surgery Off or On-pump Revascularization Study (CORONARY) that although there was a small difference in cognitive function in favor of the off-pump group at discharge, this superiority did not persist after 1 year.

Renal impairment

Contrary to what someone would expect, avoiding extracorporeal circulation does not prevent the kidney from a possible damage.[4] Indeed, randomized comparative studies between the two methods did not demonstrate any superiority of OPCAB against on-pump CABG concerning renal complications.[28,29,34,46,47] Similarly, the meta-analysis by Cheng *et al*.[22] on 3300 patients reported no statistically

significant difference between the two methods. However, Kuss *et al*.[24] showed statistically significant superiority of OPCAB with regard to renal impairment in their propensity score analyses. Same results were reported by Racz *et al*.,[14] Sabik *et al*.,[21] and Reston *et al*.,[32] who observed less renal failure requiring dialysis related to OPCAB.

Left ventricle ejection fraction

The slight postoperative improvement of the ejection fraction of the left ventricle observed does not significantly differ depending on the method used. According to Puskas *et al*.,[48] there was not a significant difference in ejection fraction improvement even at 12 months postoperatively. The ejection fraction was improved from 54% to 61% in the OPCAB group, whereas it was improved from 53% to 59% in the on-pump CABG group.

Intensive Care Unit and Hospital Stay Duration

There are controversial results regarding Intensive Care Unit (ICU) and total hospital stay after OPCAB or on-pump CABG. There are few studies that show a statistically significant superiority of OPCAB in terms of ICU stay[32,46,49] or in terms of total hospital stay.[49] A meta-analysis by Cheng *et al*.[22] reported that patients submitted to on-pump CABG had a statistically significant longer ICU stay. This was due to increased respiratory complications, increased need for respiratory support, increased intubation time, and increased need for inotropes. Racz *et al*.[14] reported a 1 day longer hospital stay when ONCAB was performed compared to OPCAB patients. On the other hand, Chu *et al*.,[18] who compared the hospital stay duration between patients submitted to OPCAB (n = 14.389) and those submitted to on-pump CABG (n = 48.658), reported longer hospital stay (by 0.6 days) when OPCAB was performed.

Mid and Long-term Outcomes

Most complaints raised against OPCAB concern the quality of peripheral anastomoses which will undoubtedly influence long-term graft patency. Indeed, there are some scientists who doubt about the quality of peripheral anastomoses and if complete revascularization is assured during OPCAB.[10] According to a retrospective study by Amano *et al*.,[11] there was a statistically significant difference in favor of on-pump CABG in terms of event-free rate at 3 years. The event-free rate at 3 years was 88% after on-pump CABG against 84% after OPCAB. Khan *et al*.[50] reported a significant superiority of OPCAB in graft patency at 3 months postoperatively (88% vs. 98%; P = 0.002). However, several randomized studies comparing long-term graft patency after OPCAB and after on-pump CABG, failed to show a statistically significant superiority of the latter.[28,48,49,51] In contrast, statistically significant greater long-term graft patency after on-pump CABG was reported by another study although it included a small number of patients.[50] A meta-analysis by Takagi *et al*.[52] showed that there is a statistically significant higher vein graft occlusion rate after OPCAB than after on-pump CABG.

Decreased need for reoperation is another indirect factor showing patency superiority. According to Hannan *et al*.,[15] patients submitted to OPCAB are significantly more prone to recurrence of angina and subsequent need for revascularization 3 years after their first revascularization operation. On the other hand, a randomized study by Puskas *et al*.,[48] including 200 patients did not show any statistically significant difference regarding graft restenosis, clinical recurrence of angina, myocardial infarction, and need for reperfusion between OPCAB and on-pump CABG. Similarly, a meta-analysis by Møller *et al*.,[10] including 15 trials with 2200 patients reported no statistically significant difference between the two methods. Feng's *et al*.[23] meta-analysis including 10 randomized trials with about 2000 patients observed no significant difference in terms of reoperation frequency at 12 months after OPCAB or on-pump CABG. More interestingly, Reston's *et al*.[32] meta-analysis showed that the recurrence of angina and subsequent need for reperfusion was higher at 3–25 months after on-pump CABG.

Conversion Rate

The need for conversion of OPCAB to conventional CABG is possible varying from 1% to 2%.[53-56] According to the recent Randomized On/Off Bypass trial,[12] including 2203 patients, the conversion rate from OPCAB to ONCAB was 12.4%, which is significantly higher than the 2.2% found in the Society of Thoracic Surgeons database. This conversion rate was even lower in the CORONARY trial (7.9%).[45] Limited surgical experience and 3-vessel disease make the conversion rate higher. Myocardial ischemia, anatomical unsuitability of the target vessel, and hemodynamic instability can be reasons why emergent intraoperative conversion should take place. Several studies have observed that emergent conversion from OPCAB to ONCAB is related to increased morbidity and mortality.[55,57-61] Mortality rates after conversion have ranged from 6% to 15%.[54,55,62-64] According to a randomized study by Légaré *et al*.,[65] out of 150 patients, 20 patients (13%) whose OPCAB operation was converted to conventional CABG, were related to significantly higher mortality rate (10% vs. 0%), higher postoperative inotropic support requirements, and higher need for transfusion. Similar results regarding mortality were reported by Patel *et al*.[66] (12% in-hospital mortality after conversion vs. 1.5% mortality without conversion) and by Jin *et al*.,[58] who observed in-hospital mortality rates as following (9.9% vs. 1.6% vs. 3.0% for converted to ONCAB patients, OPCAB patients without conversion and ONCAB patients, respectively).

Quality of Life

OPCAB has not managed to improve the quality of life compared to on-pump CABG.[34,40,67,68] According

to Puskas *et al*.,[48] although the quality of life is significantly improved at 12 months postoperatively, there is no significant difference between OPCAB and on-pump CABG. However, OPCAB was superior to on-pump CABG in terms of postoperative social functioning. No significant difference between the two methods regarding quality of life was either observed by Lamy *et al*.[45] in the CORONARY.

Cost Comparison

According to Scott *et al*.,[69] the total cost of the first surgery was significantly higher in the on-pump CABG group. According to a comparative study by Puskas *et al*.,[48] the mean cost for OPCAB- and particularly in the USA-is 17.000 dollars, whereas on-pump CABG costs 18.200 dollars on average. This difference is statistically significant in favor of OPCAB. Moreover, if this difference is calculated at 12 months postoperatively estimating possible rehospitalization, it is of the order of 1.900 dollars in favor of OPCAB.[48] On the contrary, Chu *et al*.[18] retrospectively compared the total cost of the patients' first hospitalization for OPCAB (n = 14.389) with this one for on-pump CABG (n = 48.658). The multivariable regression analysis showed a higher final cost by 1497 dollars per patient in those treated by OPCAB ($P < 0.01$).

Conclusions

Revascularization procedure without the use of extracorporeal circulation is a challenge for the surgeon. In spite of more difficult technical conditions, OPCAB offers to the patient reperfusion simultaneously preventing him from the deleterious effects of extracorporeal circulation. However, retrospective, nonrandomized, prospective randomized, and meta-analyses trials have not managed to show any significant improvement in short-term morbidity or mortality associated to OPCAB. Completeness of revascularization, technical precision, and anastomotic quality should not be compromised to avoid CPB.[1] The surgeon should choose which technique he will perform depending on the case. Indeed, subgroups such as the elderly, patients with left main stem coronary artery disease, patients with functional impairment of the left ventricle, those having a calcified aorta (porcelain aorta), those suffering from the right coronary artery disease or NSTEMI infarction, as well as patients experiencing pulmonary hypertension or pulmonary edema seem to gain profit from the OPCAB procedure.[5] High-risk subgroups such as women and diabetics may also be candidates for OPCAB.[70-72] Finally, low-risk patients do not appear to take benefit from OPCAB application compared to the conventional on-pump CABG. However, conversion to ONCAB should be avoided as it is related to increased mortality rates.

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Conflicts of interest

There are no conflicts of interest.

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